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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: P63163US0

US APPLICATION NO. (If known, see 37 CFR 1.5): [redacted]

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR98/00691	6 April 1998	9 April 1997

TITLE OF INVENTION: **SYNTHETIC PEPTIDES USEFUL IN BIOLOGICAL ASSAYS FOR DETECTING INFECTIONS CAUSED BY GROUP O HIV-1 VIRUSES**

09/147362

APPLICANT(S) FOR DO/EO/US: **Denis Marie Bernard CHENEBAUX, Jean-Francois Hubert DELAGNEAU, Stephane Jean Xavier GADELLE, Francois Yves RIEUNIER**

Applicant herein submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:

    International Search Report — EPO

    PCT Request Form

    PCT/IB/304 Form

    First Page of Publication

U.S. APPLICATION NO.(If known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
	PCT/FR98/00691	P63163US0

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (1)) $670.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (2)) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $760.00		
Neither international preliminary examination fee (37 CFR 1.492 (a) (3)) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO) **$970.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (4)) and all claims satisfied provisions of PCT Article 33(2)-(4) $96.00		
Search Report prepared by the EPO or JPO (37 CFR 1.492 (a) (5)) ... **$840.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	16 -20 =	-0-	X $18.00	$	
Independent Claims	1 -3 =	-0-	X $78.00	$	
Multiple dependent claim(s) (if applicable)			+ $260.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 840.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 840.00	
Processing fee of $130 for furnishing the English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).					
TOTAL NATIONAL FEE =				$ 840.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00				$	
TOTAL FEES ENCLOSED =				$ 840.00	
				Amount to be refunded:	$
				charged:	$

a. ☒ A check in the amount of $ 840.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. **06-1358** in the amount of $ --- to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge my account any additional fees set forth in §1.492 during the pendency of this application, or credit any overpayment to Deposit Account No. **06-1358**. A duplicate copy of this sheet is enclosed.

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By William E. Player
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JPH&S 3/95

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: CHENEBAUX et al.

Serial No.: PCT/FR 98/00691

Filed: Herewith

For: SYNTHETIC PEPTIDES USEFUL IN BIOLOGICAL ASSAYS FOR DETECTING INFECTIONS CAUSED BY GROUP O HIV-VIRUSES

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the captioned application as follows.

IN THE CLAIMS

Cancel claims 1-14, without prejudice or dicslaimer.

Add the following claims.

--**15.** Synthetic peptides of the monomer type with 13 to 33 amino acids or of the dimer type with 26 to 66 amino acids, in linear form or in a form cyclized by means of inter-cysteine disulphide bridges, having the general formula (I):

$$\Delta\text{-Z-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega \qquad \text{(I)}$$

wherein:

- Δ is selected from the group consisting of a biotinyl radical, a biocytinyl radical, a hydrogen atom, an acetyl (CH_3CO-) radical, an aliphatic chain which may contain one or two thiol, an aldehyde functional group and an amine functional group,

- Z represents a peptide sequence, selected from the group consisting of the sequences of the formulae (II) to (X):

$$-\Xi_1\text{-Ser-}\Xi_2\text{-} \qquad \text{(II)}$$

$$\text{-Ser-}\Xi_2\text{-} \qquad \text{(III)}$$

$-\Xi_1$-Ser- (IV)

$-\Xi_1$-Gln-Ξ_2- (V)

-Gln-Ξ_2- (VI)

$-\Xi_1$-Gln- (VII)

$-\Xi_1$-Asn-Ξ_2- (VIII)

-Asn-Ξ_2- (IX)

and

$-\Xi_1$-Asn- (X)

wherein:

$-\Xi_1$ represents a peptide sequence of 0 to 9 amino acids

and

$-\Xi_2$ represents a peptide sequence of 0 to 5 amino acids,

$-\Theta$ represents a peptide sequence of formula (XI):

$$-(AA_1)-(AA_2)-(AA_3)-(AA_4)-(AA_5)- \quad (XI)$$

wherein:

(AA_1) is selected from the group consisting of a lysine residue, an arginine residue, and an ornithine residue,

(AA_2) is selected from the group consisting of a glycine residue, and an asparagine residue,

(AA_3) is selected from the group consisting of a lysine residue, an arginine residue, and an ornithine residue,

(AA_4) is selected from the group consisting of a leucine residue, an alanine residue, an isoleucine residue, and a glutamine residue,

(AA_5) is selected from the group consisting of an isoleucine residue, a valine residue, a leucine residue, a threonine residue, a norleucine residue, and a norvaline residue,

provided, however, that (AA_1), (AA_2), (AA_3), (AA_4) and (AA_5) never form ogether the peptide sequences -Lys Gly Lys Leu Ile- and -Lys Gly Lys Leu Val-,

$-\Omega_1$ attached to the -CO- group of serine, is selected from the group consisting of:

- a hydroxyl (-OH) radical, an amino ($-NH_2$) radical,
- an alkoxy radical comprising from 1 to 6 carbon atoms,
- a peptide sequence of formula (XII) :

$$-Val-\Sigma-\Psi \qquad (XII)$$

wherein Σ represents a sequence selected from the group consisting of sequences of formula (XIII) and formula (XIV):

$$-(AA_6)\text{-Trp Asn-}(AA_7)\text{-}(AA_8) \qquad (XIII)$$

$$-(AA_6)\text{-Trp His-}(AA_7)\text{-}(AA_8) \qquad (XIV)$$

wherein:

(AA_6) represents an amino acid different from lysine,

(AA_7) represents an amino acid,

(AA_8) is selected from the group consisting of a serine and a threonine residue,

and Ψ, attached to the -CO- residue of the free AA_8 amino acid, is selected from the group consisting of an OH group, a NH_2 group and an alkoxy radical comprising from 1 to 6 carbon atoms,

-a peptide sequence of formula (XV):

$$-Val-\Psi \qquad (XV)$$

wherein Ψ, attached to the -CO- residue of valine, has the same meaning as for the formula (XII),

- and a peptide sequence selected from the group consisting of sequences of formula (XVI) to (XVIII):

$$-Z\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Psi \qquad (XVI)$$

$$Val-\Sigma-Z\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSerVal-}\Sigma-\Psi \qquad (XVII)$$

$$\text{and } Val-Z\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSerVal-}\Psi \qquad (XVIII)$$

wherein Z and Θ have the definition given for the formula (I) and Σ has the definition given for the formula (XII) and Ψ,

attached to the -CO- residue of serine, on the -CO- residue of the AA_8 amino acid or on the -CO- residue of valine, has the same meaning as for the formula (XII).

16. Synthetic peptides of formula (I) according to claim 15 wherein Δ represents an aliphatic chain, said aliphatic chain being selected from the group consisting of an alkyl chain of 1 to 6 carbon atoms, an alkenyl chain of 2 to 6 carbon atoms, and an aminoalkylcarbonyl chain of 2 to 6 carbon atoms.

17. Synthetic peptides of formula (I) according to claim 15, wherein (AA_5) is selected from the group consisting of a valine residue, a leucine residue, and a threonine residue and when Ω corresponds to a peptide sequence of formula (XII) or (XIV), (AA_6) is selected from the group consisting of a glutamine residue and an arginine residue.

18. Synthetic peptides of formula (I), according to claim 15, wherein:

-Δ is selected from the group consisting of a biotinyl radical, a hydrogen atom, an aliphatic chain which may contain one or two thiol, an aldehyde functional group and an amine functional group,

-Z represents a peptide sequence of formula (II) or (V), wherein Ξ_1 represents a peptide sequence of two amino acids and Ξ_2 represents an amino acid, or a sequence of formula (IV), wherein Ξ_1 represents three amino acids, or a peptide sequence of formula (VIII), wherein Ξ_1 represents a peptide sequence of nine, eight or three amino acids and $_{\Xi 2}$ a peptide sequence of five amino acids,

-Θ is selected from the group consisting of peptide sequences of formulae:

-Lys Gly Arg Leu Val-,

-Arg Gly Lys Ala Val-,

- Arg Gly Arg Leu Val-, and

-Arg Gly Arg Ala Val-,

and

-Ω is selected from the group consisting of a hydroxyl group, the peptide sequence (XV) and one of the following sequences representing the peptide sequence of formula (XII):

- Val Arg Trp Asn Glu Thr-Ψ,
- Val Gln Trp Asn Glu Thr-Ψ and
- Val Gln Trp Asn Ser Thr-Ψ.

19. Synthetic peptides of formula (I), according to claim 15, wherein Z is selected from the group consisting of peptide sequences of formulae:

-Leu Leu Ser Ser-

-Leu Leu Asn Ser-

-Arg Leu Asn Ser-

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser-

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu-

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile-

-Leu Asn Gln Gln Arg Leu Leu Asn Ser-

and

-Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser-.

20. Synthetic peptides of 20 to 50 amino acids according to claim 15, of formula (Ia):

$$\Delta\text{-}Z_a\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega_a \qquad \text{(Ia)}$$

wherein Z_a is selected from the group consisting of radicals of formulae IIa to Xa:

Ξ_{1a}-Ser-Ξ_{2a} (IIa)

-Ser-Ξ_{2a} (IIIa)

Ξ_{1a}-Ser (Iva)

Ξ_{1a}-Gln-Ξ_{2a} (Va)

-Gln-Ξ_{2a} (VIa)

Ξ_{1a}-Gln- (VIIa)

Ξ_{1a}-Asn-Ξ_{2a} (VIIIa)

-Asn-Ξ_{2a} (Ixa)

-Ξ_{1a}-Asn (Xa)

wherein:

-Ξ_{1a} represents a peptide sequence of 1 to 5 amino acids

and

-Ξ_{2a} an amino acid,

-Ω_a represents a peptide sequence of formula (XII), as defined for the formula (I), or a peptide sequence of formula (XVIIa):

Val-Σ-Z_a-TrpGlyCys-Θ-CysTyrThrSerVal-Σ-Ψ (XVIIa)

and

Δ, Θ, Σ and Ψ have the same meaning as for the formula (I).

21. Synthetic peptides of formula (I) according to claim 15 including one of the following sequences:

Sequence No. 1

-LLSLWGCRGKAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 2

-LLSLWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 3

-LLSSWGCKGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 4

-LLSSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Ser Thr-

22

Sequence No. 5

-LLQSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu alV Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Ser Thr-

22

Sequence No. 6

-LLNSWGCRGKAVCYTSVQWNET-

or

-Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 7

-LLSLWGCRGRAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 8

-LLSSWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr-

22

Sequence No. 9:

-LLSSWGCKGRLVCYTS-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-

1 5 10 15

Sequence No. 10:

-LLNSWGCKGRLVCYTS-

or

-Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-

1 5 10 15

Sequence No. 11:

-ALETLLQNQQLLNSWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-

20 25 30

Sequence No. 12:

-ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-

20 25 30

Sequence No. 13:

-ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-

20 25 30

Sequence No. 14:

-LNQQRLLNSWGCKGRLVCYTSV-

or

-Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr
1 5 10 15

Thr Ser Val-
20

Sequence No. 15:

-RALETLLNQQRLLNSWGCKGRLVCYTSV-

or

- Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys
1 5 10 15

Gly Arg Leu Val Cys Tyr Thr Ser Val-
20 25

Sequence No. 16:

-RLNSWGCKGRLVCYTSV-

or

- Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val-
1 5 10 15

22. Synthetic peptides, according to claim 15, of sequence:

PEPTIDE No. 1 (2B)

LLSLWGCRGKAVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr

22

PEPTIDE No. 2 (3B)

LLSLWGCRGRLVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr

22

PEPTIDE No. 3 (4B)

LLSSWGCKGRLVCYTSVQWNET

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Glu Thr

22

PEPTIDE No. 4 (5B)

LLSSWGCKGRLVCYTSVQWNST

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn

1 5 10 15 20

Ser Thr

22

PEPTIDE No. 5 (6B)

LLQSWGCKGRLVCYTSVQWNST

or

Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr
22

PEPTIDE No. 6

LLNSWGCRGKAVCYTSVQWNET

or

Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 7

LLSLWGCRGRAVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 8 (7B)

LLSSWGCRGRLVCYTSVQWNET

or

Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 9 (12B)

LLSSWGCKGRLVCYTS

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

PEPTIDE No. 10 (14B)

LLNSWGCKGRLVCYTS

or

Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

PEPTIDE No. 11 (18B)

ALETLLQNQQLLNSWGCRGRLVCYTSVRWNET

or

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE NO. 12 (19B)

ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET

or

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE No. 13 (20B)

ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr

20 25 30

PEPTIDE No. 14 (21B)

LNQQRLLNSWGCKGRLVCYTSV

or

Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr

1 5 10 15

Thr Ser Val

20

PEPTIDE No. 15 (22B)

RALETLLNQQRLLNSWGCKGRLVCYTSV

or

Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys

1 5 10 15

Gly Arg Leu Val Cys Tyr Thr Ser Val

20 25

PEPTIDE No. 16 (23B)

RLNSWGCKGRLVCYTSV

or

Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val

1 5 10 15

23. Composition containing at least one synthetic peptide of formula (I) according to claim 15.

24. Composition according to claim 21 containing peptide No. 3 (4B) and peptide No. 1 (2B).

25. Composition containing at least one synthetic peptide of formula (I) according to claim 15 and at least one group O HIV-1 recombinant peptides.

26. Composition containing at least one synthetic peptide of formula (I), according to claim 15, and at least one HIV-1 and/or HIV-2 recombinant or synthetic peptide.

27. Immunoassay method comprising the steps of:

1) contacting at least one synthetic peptide of formula (I) according to claim 15, previously detectably labelled, with a sample likely to contain antibodies directed to said peptides;

2) detecting the presence of a complex between said peptides and said antibodies;

3) optionally assaying the amount of said antibodies in the sample.

28. Immunoassay method comprising the steps of:

1) contacting a composition according to claim 23, containing at least one synthetic peptide of formula (I), previously detectably labelled, with a sample likely to contain antibodies directed to said peptides;

2) detecting the presence of a complex between said peptides and said antibodies;

3) optionally assaying the amount of said antibodies in the sample.

29. Diagnostic kit including at least one synthetic peptide of formula (I), according to claim 15.

30. Diagnostic kit including a composition according to claim 23.--

REMARKS

The instant amendment eliminates multiple dependencies in order to reduce the filing fee.

Favorable action commensurate with the foregoing is requested.

Respectfully submitted,

William E. Player
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Atty. Docket No.: 10496/P63163US0

WEP:dlb

S:\HOME\CBROWN\NOV\P63163.PRE

" Synthetic peptides useful in biological essays for detecting infections caused by group O HIV-1 viruses"

The invention relates to synthetic peptides which can be used in biological tests for the detection of infections due to the group O HIV-1 viruses, to the method for preparing them, to compositions and kits containing such peptides and to the biological tests using such peptides.

Group O HIV-1 retroviruses are known in the prior art. Patent EP 0,345,375 and patent application EP 0,657,532 describe the ANT 70 and ANT 70 NA isolates isolated from Cameroonian patients. These documents describe more precisely antigens and antigenic compositions containing lysates or proteins of these isolates, the nucleic acids corresponding to the genomic RNA, hybridization methods using these nucleic acids, methods of producing the isolates indicated above as well as methods of preparing p12, p16, p25, gp41 and gp120 proteins of these retroviruses.

Application EP 0,591,914 describes the MVP 5180/91 isolate. This isolate, characterized by Western blotting, exhibits, like the previous isolate, differences in relation to the HIV-1 retrovirus isolates which have been known for a long time. Application EP 0,591,914 describes precisely the DNA sequence of the MVP 5180/91 isolate and indicates precisely the location of the gag, pol and env genes. Application EP 0,591,914 further describes synthetic peptides of the V3 loop as well as the immunodominant region (gp41). They are useful for biological tests, in particular for the *in vitro* detection of group O HIV-1 antibodies.

Application EP 0,673,948 describes synthetic or recombinant peptides consisting of 15 to 50 amino acids (AA) and comprising the sequence

-VWGIRQLRARLQALETLIQNQQRLNLWG**X**KGKLI**X**YTSVKWNTSWSGR-

in which X represents either a cysteine residue, or a serine residue These peptides are useful in the diagnostic field for the detection of infections due to certain group O HIV-1 retrovirus isolates.

Application EP 0,727,483 is also known which describes the MVP 2901/94 isolate which also forms part of the retroviruses belonging to the group O HIV-1 family. This application describes certain antigens having well-determined peptide sequences. These peptide sequences correspond to part of the sequence of gp120 and part of gp41 (immunodominant region) of the MVP 2901/94 isolate.

Application WO 96/12809 describes two new isolates belonging to the group O HIV-1 family. They are the VAU and DUR isolates. This application describes certain peptide sequences derived from the two viruses cited above, which are useful for the detection of antibodies recognizing the HIV-1 VAU or DUR peptide sequences.

Application WO 96/32293 describes two antigens derived from the sequence of the ANT 70 isolate. They are the antigen called MDL061 and the antigen MDL056, of the immunodominant region of gp41. According to this invention, to detect 100% of the samples of a limited collection of sera from patients infected with the group O HIV-1 virus, it is necessary to use compositions containing these two peptides, since each isolated peptide does not allow, on its own, satisfactory results to be obtained.

Indeed, it is practically impossible, in the light of the genetic variability shown by the isolates of the group O virus, to guarantee serological screening of individuals infected by the use of antigens derived from the same and sole isolate. This means that it is not possible to obtain reagents which guarantee 100% sensitivity. The O group thus raises, for the first time, a major problem; it is the inability of certain serological reagents to recognize individuals infected with particularly divergent groups or subtypes. This is precisely the case for the group O HIV-1 viruses.

Application WO 96/40763 also stresses the great divergence of the O group. This application describes peptides which incorporate, into a natural HIV-1 type B sequence, a few minor modifications (replacement of one or two amino acids). According to this application, these hybrid peptides are capable of reacting with anti-group O antibodies.

Application WO 96/27013 describes a series of new group O HIV-1 viruses designated BCF 01, BCF 02, BCF 03, BCF06, BCF 07, BCF 08, BCF09, BCF11, BCF12, BCF13 and BCF14 as well as a series of peptides of the corresponding gp41 dominant region which are called ESS/BCF02, FAN/BCF01, LOB/BCF06, MAN/BCF07, NKO/BCF08, POC/BCF03, NAN/BCF11, BCF09, BCF12, BCF13 and BCF14. A number of these peptides are difficult to handle in diagnosis because of their low solubility, especially the peptide BCF13.

Unexpectedly, it has now been found that certain synthetic peptides are diagnostic reagents of superior quality and they make it possible to satisfactorily screen patients infected with group O HIV-1 retroviruses. These peptides are composed of variable sequences articulated around highly conserved short sequences, which are present in isolates of the group O HIV-1 retroviruses. The peptides of the invention make it possible to obtain results which are quite superior to those obtained with synthetic peptides carrying immunodominant epitopes of the gp41 (env) of certain group O HIV-1 isolates.

Subsequently, to name the amino acids, the three-letter nomenclature will be used.

The synthetic peptides of the invention correspond to the general formula (I):

$$\Delta\text{-Z-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega \qquad (I)$$

in which :

-Δ represents a biotinyl radical, a biocytinyl radical, a hydrogen atom, an acetyl (CH_3CO-) radical, an aliphatic chain which may contain one or two thiol, aldehyde or amine functional groups, the aliphatic chain preferably being an alkyl chain of 1 to 6 carbon atoms or an alkenyl chain of 2 to 6 carbon atoms, or an aminoalkylcarbonyl chain of 2 to 6 carbon atoms,

-Z represents a peptide sequence of one of the formulae (II) to (X) :

$-\Xi_1$-Ser-Ξ_2-	(II)
-Ser-Ξ_2-	(III)
$-\Xi_1$-Ser-	(IV)
$-\Xi_1$-Gln-Ξ_2-	(V)
-Gln-Ξ_2-	(VI)
$-\Xi_1$-Gln-	(VII)
$-\Xi_1$-Asn-Ξ_2-	(VIII)
-Asn-Ξ_2-	(IX)
Ξ_1-Asn-	(X)

in which :

-Ξ_1 represents a peptide sequence of 0 to 9 amino acids and

-Ξ_2 represents a peptide sequence of 0 to 5 amino acids,

-Θ represents a peptide sequence of formula (XI):

$-(AA_1)-(AA_2)-(AA_3)-(AA_4)-(AA_5)-$ (XI)

in which :

- (AA_1) represents either a lysine residue, or an arginine residue, or an ornithine residue,
- (AA_2) represents either a glycine residue, or an asparagine residue,
- (AA_3) represents either a lysine residue, or an arginine residue, or an ornithine residue,
- (AA_4) represents either a leucine residue, or an alanine residue, or an isoleucine residue, or a glutamine residue,

- (AA_5) represents either an isoleucine residue, or a valine residue, or a leucine residue, or a threonine residue, or a norleucine residue, or a norvaline residue,

provided, however, that (AA_1), (AA_2), (AA_3), (AA_4) and (AA_5) never form together the peptide sequences -Lys Gly Lys Leu Ile- and -Lys Gly Lys Leu Val-,

-Ω, attached to the -CO- group of serine, represents:

- a hydroxyl (-OH) radical or an amino ($-NH_2$) radical,
- an alkoxy radical comprising from 1 to 6 carbon atoms,
- a peptide sequence of formula (XII) :

-Val-Σ-Ψ (XII)

in which Σ represents a sequence of formula (XIII) or of formula (XIV) :

-(AA_6)-Trp Asn-(AA_7)-(AA_8) (XIII)

-(AA_6)-Trp His-(AA_7)-(AA_8) (XIV)

in which :

- (AA_6) represents an amino acid different from lysine,
- (AA_7) represents an amino acid,
- (AA_8) represents a serine or threonine residue,

and Ψ, attached to the -CO- residue of the free AA_8 amino acid, represents an OH or NH_2 group or an alkoxy radical comprising from 1 to 6 carbon atoms,

- a peptide sequence of formula (XV) :

-Val-Ψ (XV)

in which Ψ, attached to the -CO- residue of valine, has the same meaning as for the formula (XII),

- or a peptide sequence of one of the formulae (XVI) to (XVIII) :

-Z-TrpGlyCys-Θ-CysTyrThrSer-Ψ (XVI)

Val-Σ-Z-TrpGlyCys-Θ-CysTyrThrSerVal-Σ-Ψ (XVII)

Val-Z-TrpGlyCys-Θ-CysTyrThrSerVal-Ψ (XVIII)

in which Z and Θ have the definition given for the formula (I)

and Σ has the definition given for the formula (XII) and Ψ, attached to the -CO- residue of serine, on the -CO- residue of the AA_8 amino acid or on the -CO- residue of valine, has the same meaning as for the formula (XII).

When Ω represents a peptide sequence of one of the formulae (XVI) to (XVIII), the peptide of formula (I) becomes a dimer whose size may vary from 26 to 66 amino acids. When Ω does not represent a peptide sequence of one of the formulae (XVI) to (XVIII), the peptides of formula (I) are of the monomeric type and their size may vary from 13 to 33 amino acids.

The peptides according to the invention may be either in a linear form, or in a form cyclized by means of inter-cysteine disulphide bridges.

The compounds of formula (I) in which (AA_5) represents either a valine residue, or a leucine residue, or a threonine residue are preferred, and when Ω corresponds to a peptide sequence of formula (XII), (AA_6) represents either a glutamine residue or an arginine residue.

The peptides of formula (I) are preferred in which:

-Δ represents a biotinyl radical, a hydrogen atom or an aliphatic chain which may contain one or two thiol, aldehyde or amine functional groups, the aliphatic chain preferably being an alkyl chain of 1 to 6 carbon atoms, or an aminoalkylcarbonyl chain of 2 to 6 carbon atoms,

-Z represents a peptide sequence of formula (II) or (V), in which Ξ_1 represents a peptide sequence of two amino acids and Ξ_2 represents an amino acid, or a sequence of formula (IV), in which Ξ_1 represents three amino acids, or a peptide sequence of formula (VIII), in which Ξ_1 represents a peptide sequence of nine, eight or three amino acids and Ξ_2 a peptide sequence of five amino acids,

-Θ represents a peptide sequence of formula:

-Lys Gly Arg Leu Val-,

-Arg Gly Lys Ala Val-,

- Arg Gly Arg Leu Val-,

or

-Arg Gly Arg Ala Val-,

and

-Ω represents a hydroxyl group, the peptide sequence (XV) or one of the following sequences which correspond to the peptide sequence of formula (XII) :

- Val Arg Trp Asn Glu Thr-Ψ,

- Val Gln Trp Asn Glu Thr-Ψ

or

- Val Gln Trp Asn Ser Thr-Ψ.

Preferably, Z represents a peptide sequence of formula:

- -Leu Leu Ser Ser-
- -Leu Leu Asn Ser-
- -Leu Leu Gln Ser-
- -Arg Leu Asn Ser-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile-
- -Leu Asn Gln Gln Arg Leu Leu Asn Ser-

or

- -Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser-

Also forming part of the invention are the synthetic peptides comprising from 20 to 50 amino acids and corresponding to the formula (Ia) :

$$\Delta\text{-}Z_a\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega_a \qquad \text{(Ia)}$$

in which Z_a represents a radical of formulae IIa to Xa :

Ξ_{1a}-Ser-Ξ_{2a} (IIa)

-Ser-Ξ_{2a} (IIIa)

-Ξ_{1a}-Ser (IVa)

Ξ_{1a}-Gln-Ξ_{2a} (Va)

-Gln-Ξ_{2a} (VIa)

Ξ_{1a}-Gln- (VIIa)

Ξ_{1a}-Asn-Ξ_{2a} (VIIIa)

-Asn-Ξ_{2a} (IXa)

-Ξ_{1a}-Asn (Xa)

in which :

-Ξ_{1a} represents a peptide sequence of 1 to 5 amino acids

and

-Ξ_{2a} an amino acid,

-Ω_a represents a peptide sequence of formula (XII), as defined for the formula (I), or a peptide sequence of formula (XVIIa) :

Val-Σ-Z_a-TrpGlyCys-Θ-CysTyrThrSerVal-Σ-Ψ (XVIIa)

in which Z_a has the meaning given for the formula (Ia)

and

Δ, Θ, Σ and Ψ have the same meaning as for the formula (I).

The peptides of formula (I) or (Ia) including one of the following sequences (these peptides may be of the dimer type or of the monomer type as defined above) are preferred. The sequences are given according to the one- and three-letter nomenclatures:

Sequence No. 1

-LLSLWGCRGKAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 2

-LLSLWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 3

-LLSSWGCKGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 4

-LLSSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr-
22

Sequence No. 5

-LLQSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr-
22

Sequence No. 6

-LLNSWGCRGKAVCYTSVQWNET-

or

-Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 7

-LLSLWGCRGRAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 8

-LLSSWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 9 :

-LLSSWGCKGRLVCYTS-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-

1 5 10 15

Sequence No. 10 :

-LLNSWGCKGRLVCYTS-

or

-Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-

1 5 10 15

Sequence No. 11 :

-ALETLLQNQQLLNSWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-

20 25 30

Sequence No. 12 :

-ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-

20 25 30

Sequence No. 13 :

-ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-
20 25 30

Sequence No. 14 :

-LNQQRLLNSWGCKGRLVCYTSV-

or

-Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr
1 5 10 15
Thr Ser Val-
20

Sequence No. 15 :

-RALETLLNQQRLLNSWGCKGRLVCYTSV-

or

- Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys
1 5 10 15
Gly Arg Leu Val Cys Tyr Thr Ser Val-
20 25

Sequence No. 16 :

-RLNSWGCKGRLVCYTSV-

or

- Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val-
1 5 10 15

The synthetic peptides below are particularly preferred peptides:

PEPTIDE No. 1 (2B) : SEQ ID No. 1

LLSLWGCRGKAVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 2 (3B) : SEQ ID No. 2

LLSLWGCRGRLVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 3 (4B) : SEQ ID No. 3

LLSSWGCKGRLVCYTSVQWNET

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 4 (5B) : SEQ ID No. 4

LLSSWGCKGRLVCYTSVQWNST

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr
22

PEPTIDE No. 5 (6B) : SEQ ID No. 5

LLQSWGCKGRLVCYTSVQWNST

or

Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr
22

PEPTIDE No. 6 : SEQ ID No. 6

LLNSWGCRGKAVCYTSVQWNET

or

Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 7 : SEQ ID No. 7

LLSLWGCRGRAVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 8 (7B) : SEQ ID No. 8

LLSSWGCRGRLVCYTSVQWNET

or

Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 9 (12B) : SEQ ID No. 9

LLSSWGCKGRLVCYTS

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

PEPTIDE No. 10 (14B) : SEQ ID No. 10

LLNSWGCKGRLVCYTS

or

Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

PEPTIDE No. 11 (18B) : SEQ ID No. 11

ALETLLQNQQLLNSWGCRGRLVCYTSVRWNET

or

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE No. 12 (19B) : SEQ ID No. 12

ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET

or

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE No. 13 (20B) : SEQ ID No. 13

ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly

1 5 10 15

Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr

20 25 30

PEPTIDE No. 14 (21B) : SEQ ID No. 14

LNQQRLLNSWGCKGRLVCYTSV

or

Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr

1 5 10 15

Thr Ser Val

20

PEPTIDE No. 15 (22B) : SEQ ID No. 15

RALETLLNQQRLLNSWGCKGRLVCYTSV

or

Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys

1 5 10 15

Gly Arg Leu Val Cys Tyr Thr Ser Val

20 25

PEPTIDE No. 16 (23B) : SEQ ID No. 16

RLNSWGCKGRLVCYTSV

or

Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val

1 5 10 15

The synthetic peptides of formula (I), which are the subject of the present invention, can be obtained by solid phase synthesis according to conventional methods: R.B. Merrifield, *J. Amer. Chem. Soc. (1963), 85,*

pp. 2149-2154 ; R.C. Sheppard, *in " Peptides 1971 ", Nesvadba H. (ed.) North Holland, Amsterdam, pp. 111* ; E. Atherton and R.L. Sheppard, *in " Solid phase peptide synthesis, a practical approach ", IRL PRESS, (1989), Oxford University Press, pp. 25-34.* As automatic synthesizer, it is possible to use the synthesizer " 9050 Plus Pep Synthesizer " from Millipore or an equivalent synthesizer.

The solid support used for the syntheses should be compatible with the technique and the chemistry used. For example, for a synthesis on the synthesizer " 9050 Plus pep. Synthesizer ", it is recommended to use a resin suitable for the so-called "continuous flow" technique; the PEG PS resins meet these criteria. These supports consist of an arm ("spacer") based on polyethylene glycol (PEG) situated between the functional group of the polystyrene beads and the point of attachment of the first amino acid. The nature of this point of anchorage may vary according to the C-terminal functional group chosen. In the present case, various PEG-PS resins were used.

The starting resin and the amino acids used as raw materials are products which are commercially available (PerSeptive-Biosystem, or Neosystem).

For the peptide synthesis, the following side chain protecting groups were used:

Amino acids	Protecting group
Arginine	Pentamethyl-2,2,4,6,7-dihydrobenzofuran-5-sulphonyl (Pbf)
Asparagine, Glutamine	Trityl (Trt)
Cysteine	Trityl (Trt) or Acetamidomethyl (Acm)
Serine, Threonine, Tyrosine	tert-Butyl ether (tBu)
Lysine, Tryptophan	tert-Butyloxycarbonyl (Boc)

The temporary protection of the primary amine functional group at the α position of the amino acids which is used is the 9-fluorenylmethyloxylcarbonyl (Fmoc) group. The deprotection is carried out with a 20% solution of piperidine in dimethylformamide.

For the coupling, an excess of diisopropylcarbodiimide (DIPCDI) and 1-hydroxybenzotriazole (HOBt) is preferably used.

After synthesis, the resin is washed with organic solvents (dimethylformamide, followed by dichloromethane), dried under vacuum and then treated with a trifluoroacetic acid (TFA)-based solution cooled to 0°C and containing appropriate " scavengers ". There may be used, for example, the K reagent containing 82% of trifluoroacetic acid, 5% of phenol, 5% of water, 5% of thioanisole and 3% of ethanedithiol.

After filtration of the resin, the synthetic peptides are precipitated and rinsed with ether.

The synthetic peptides are then purified by reversed phase liquid chromatography and their purity is determined by mass spectrometry. As solid phase, it is possible to use, for example, the Bondapak C-18 phase. The peptides are eluted by forming a linear gradient between two buffer solutions, the first which is essentially aqueous (for example water-TFA 0.1%) and the second which is rather organic (for example a mixture containing 60% acetonitrile, 39.92% water and 0.08% TFA). The pure fractions collected are combined, concentrated under vacuum and freeze-dried.

For the cyclization, the purified synthetic peptides are dissolved in an ammonium acetate solution (10 mM). The pH is adjusted to 8.5 by addition of 1 M ammonium hydroxide. The solution is vigorously stirred.

The cyclization is complete after 18 hours. The pH is then reduced to 6 by addition of acetic acid. The cyclized peptides are freeze-dried and then purified by reversed phase liquid chromatography as described above.

The immunoreactivity of the peptides of the invention was evaluated with the aid of sera from patients predominantly of Cameroonian origin infected with group O HIV-1 retroviruses. The various tests carried out demonstrated that the peptides of the invention, alone or in combination (compositions of peptides), make it possible to detect 100% of the sera infected with group O HIV-1 retroviruses.

The synthetic peptides of the invention therefore find application in immunological tests for the screening of infections due to group O HIV-1 retroviruses. It is also possible to use combinations of several synthetic peptides of formula I. These combinations, which may contain two or more peptides of formula I, also form part of the invention. Combinations containing peptides No. 1 (2B) and No.3 (4B) are preferred.

It is also possible to use synthetic peptides of formula (I) of the present invention in combination with group O HIV-1 recombinant peptides (recombinant proteins) as can be obtained by conventional methods and having the sequences described, for example in application EP 0,591,914. Such compositions are also within the scope of the present invention.

The synthetic peptides of the invention can also be used in combination with other HIV-2 and/or HIV-1 recombinant (recombinant proteins) or synthetic peptides, such as the peptides described in patent applications or patents EP 0,387,914, EP 0,239,425, EP 0,220,273 or EP 0,267,802. This list of patent applications or patents is not exhaustive and is given by way of example.

The compositions containing one or more synthetic peptides of

formula (I) and one or more HIV-1 or HIV-2 recombinant or synthetic peptides find application in diagnosis for the screening of patients infected with various HIV retroviruses. These compositions also form part of the present invention.

Immunoassay methods using one or more synthetic peptides of formula (I), alone or in combination with group O HIV-1 recombinant peptides or HIV-1 and/or HIV-2 recombinant or synthetic peptides, also form part of the invention.

The invention also relates to kits, for carrying out immunoassays, which include a peptide of formula (I) or a composition which contains at least one peptide of formula (I).

The following examples illustrate the invention and are given with no limitation being implied.

EXAMPLE 1 :

Preparation of a compound according to the invention; PEPTIDE No. 2 (3B)

LLSLWGCRGRLVCYTSVQWNET

or

Leu	Leu	Ser	Leu	Trp	Gly	Cys	Arg	Gly	Arg	Leu	Val	Cys	Tyr	Thr	Ser	Val	Gln	Trp	Asn
1				5					10					15					20

Glu	Thr
	22

This peptide was synthesized on a solid phase. The technique developed in 1963 by Merrifield *(J. Am. Chem. Soc. (1963) 85, pp. 2149-2154)* consists in attaching the first amino acid onto a polymeric solid support (resin) by its acid functional group and in extending the peptide sequence from this first amino acid, the peptide being synthesized remaining anchored on the resin.

For the synthesis of peptide No. 2, there were used, as synthesizer, the synthesizer " 9050 Plus Pep Synthesizer " and as resin, the resin Fmoc Thr (OtBu) PEG PS.

The various steps of the synthesis are summarized in Table I below:

Table I

AMINO ACID RESIDUE	NH_2 PROTECTION	SIDE PROTECTION	COUPLING METHOD	EQ NUMBER - DURATION OF COUPLING
Glu	Fmoc	OtBu	DIPCDI/HOBt	5 eq - 30 min
Asn	Fmoc	Trt	DIPCDI/HOBt	5 eq - 30 min
Trp	Fmoc	Boc	DIPCDI/HOBt	5 eq - 30 min
Gln	Fmoc	Trt	DIPCDI/HOBt	5 eq - 30 min
Val	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Ser	Fmoc	tBu	DIPCDI/HOBt	5 eq - 30 min
Thr	Fmoc	tBu	DIPCDI/HOBt	5 eq - 30 min
Tyr	Fmoc	tBu	DIPCDI/HOBt	5 eq - 30 min
Cys	Fmoc	Trt	DIPCDI/HOBt	5 eq - 30 min
Val	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Leu	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Arg	Fmoc	Pbf	DIPCDI/HOBt	5 eq - 30 min
Gly	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Arg	Fmoc	Pbf	DIPCDI/HOBt	5 eq - 30 min
Cys	Fmoc	Trt	DIPCDI/HOBt	5 eq - 30 min
Gly	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Trp	Fmoc	Boc	DIPCDI/HOBt	5 eq - 30 min
Leu	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Ser	Fmoc	tBu	DIPCDI/HOBt	5 eq - 30 min
Leu	Fmoc		DIPCDI/HOBt	5 eq - 30 min
Leu	Fmoc		DIPCDI/HOBt	5 eq - 30 min

At the end of the synthesis, the resin was washed with dimethylformamide and then dichloromethane and dried under vacuum.

Next, the resin was treated with the K reagent (82% trifluoroacetic acid; 5% phenol; 5% water; 5% thioanisole; 3% ethanedithiol). Peptide No. 2 (3B), isolated by precipitation with the aid of diethyl ether, was then rinsed with the same solvent. 140 mg of peptide No. 2 (3B) were thus obtained.

Peptide No. 2 (3B) was then purified by reversed phase liquid chromatography. The Bondapak C-18 phase was used as solid phase. The peptide was eluted by forming a linear gradient between two buffer solutions, the first which is essentially aqueous (for example water-TFA 0.1%) and the second which is rather organic (for example a mixture containing: 60% acetonitrile, 39.92% water and 0.08% TFA). The pure fractions collected were combined, concentrated under vacuum and freeze-dried.

For the cyclization, the purified synthetic peptide thus obtained was dissolved in an ammonium acetate solution (10 mM). The pH was adjusted to 8.5 by addition of 1 M ammonium hydroxide. The solution was vigorously stirred. The cyclization was complete after 18 hours. The pH was then reduced to 6 by addition of acetic acid. The cyclized peptide was freeze-dried and then purified by reversed phase liquid chromatography as described above.

Preparation of a compound according to the invention: PEPTIDE No. 15 (22B)

This peptide was synthesized as peptide No. 2 (3B), but using as resin the resin FmocPAL PEG-PS.

The various steps of the synthesis are summarized in Table III

below:

Table II

AMINO ACID RESIDUE	NH_2 PROTECTION	SIDE PROTECTION	COUPLING METHOD	EQ NUMBER - DURATION OF COUPLING
Val	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Ser	Fmoc	tBu	DIPCDI/HOBt	5 eq - 45 mn
Thr	Fmoc	tBu	DIPCDI/HOBt	5 eq - 45 mn
Tyr	Fmoc	tBu	DIPCDI/HOBt	5 eq - 45 mn
Cys	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Val	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Arg	Fmoc	Pbf	DIPCDI/HOBt	5 eq - 45 mn
Gly	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Lys	Fmoc	Boc	DIPCDI/HOBt	5 eq - 45 mn
Cys	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Gly	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Trp	Fmoc	Boc	DIPCDI/HOBt	5 eq - 45 mn
Ser	Fmoc	tBu	DIPCDI/HOBt	5 eq - 45 mn
Asn	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Arg	Fmoc	Pbf	DIPCDI/HOBt	5 eq - 45 mn
Gln	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Gln	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Asn	Fmoc	Trt	DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Thr	Fmoc	tBu	DIPCDI/HOBt	5 eq - 45 mn
Glu	Fmoc	OtBu	DIPCDI/HOBt	5 eq - 45 mn
Leu	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Ala	Fmoc		DIPCDI/HOBt	5 eq - 45 mn
Arg	Fmoc	Pbf	DIPCDI/HOBt	5 eq - 45 mn

At the end of the synthesis, the resin was washed with dimethylformamide, followed by dichloromethane and dried under vacuum.

Next, the resin was treated with the K reagent (82% trifluoroacetic acid; 5% phenol; 5% water; 5% thioanisole; 3% ethanedithiol). The peptide No.7 (22B) isolated by precipitation with the aid of diethyl ether was then rinsed with the same solvent. 140 mg of peptide No. 15 (22B) were thus obtained.

Peptide No. 15 (22B) was then purified by reversed phase liquid chromatography and then cyclized, freeze-dried and purified as described above for peptide No. 2 (3B).

In the same manner, and using the appropriate resins and amino acids, the other compounds of the invention were synthesized.

Table III indicates the molecular weight of some peptides of formula (I), in non-cyclized form, evaluated by mass spectrometry.

Table III

Peptide No.	Molecular weight (Daltons)
1 (2B)	2512
2 (3B)	2583
3 (4B)	2528
4 (5B)	2586
5 (6B)	2527
9 (12B)	1772
10 (14B)	1799
11 (18B)	3752
12 (19B)	3778
13 (20B)	3780
14 (21B)	2538
15 (22B)	3222
16 (23B)	1941

EXAMPLE 2 :

Evaluation of the immunoreactivity of the peptides according to the invention by the immunoenzymatic test: Test No. 1

The sera used ESS, DUR, VAU and HAD are sera from French patients infected with group O HIV-1 retroviruses. The other serum samples from patients infected with group O HIV-1 retroviruses were obtained by the Yaoundé Pasteur Centre in Cameroon and were serotyped group O according to the serological algorithm described in *AIDS (1977), 11, pp 445-453.*

The HIV-negative sera (n=48) were obtained from healthy

volunteers.

The synthetic peptides used were dissolved in water at a concentration of 1 mg/ml (stock solution). For the solid phase sensitization step (coating), 110 µl of a solution at 2 µg/ml of each peptide (obtained by diluting the stock solution with 0.1 M carbonate buffer solution) were added to each well of the microtitre plates Microtiter™ (NUNC). After incubating overnight at room temperature, the microplates were first washed with a Tris-NaCl buffer solution pH 7.4 containing 0.1% of Tween® 20 and 0.001% sodium merthiolate, and then saturated with a PBS solution containing 0.5% of Régilait™ (dried skimmed milk). After aspirating the saturating solution, the plates were heated for 10 min at 50°C.

The serum samples were diluted 1/5 with a skimmed milk solution (citrate buffer supplemented with 0.01% of phenol red, 0.25% of chloroform and 0.25% of Kathon®), deposited in the wells of the plates and incubated for 30 min at 40°C.

After washing with a Tris-NaCl buffer solution pH 7.4 containing 0.1% of Tween® 20 and 0.001% of sodium merthiolate, 100 µl of a solution of conjugate consisting of horseradish peroxidase-labelled anti-human IgG and IgM goat antibodies, containing as preservative 0.01% of sodium merthiolate, in solution in a citrate buffer solution supplemented with 30% glycerol and 25% normal foetal calf serum, were added to each plate well and then the plates were incubated for 30 min at 40°C.

After washing with a Tris-NaCl buffer solution pH 7.4 containing 0.1% of Tween® 20 and 0.001% of sodium merthiolate, the colour was developed by adding, to each well, 100 µl of O-phenylenediamine in solution in hydrogen peroxide. The microplates were then incubated for 30 min at room temperature and in the dark. The coloured reaction was then stopped by addition of 100 µl of 4N sulphuric acid. The absorbance (A)

was determined at 490 and 620 nm.

The relative absorbance (A490-A620) read in each well is proportional to the immunoreactivity of each peptide. It indicates the ability of each peptide to react with the biological sample with which the test is carried out. The cut-off value was determined as being an absorbance equal to 0.15. It corresponds to the mean of the negative values (n=48) plus 12 standard deviations.

The reactivity of the peptides of the invention (peptide No. 3 (4B), peptide No. 2 (3B) and peptide No. 1 (2B), all in cyclized form), was compared with that of two synthetic peptides having, as sequence, a portion of the natural sequence of the envelope (env) of the VAU isolate (group O HIV-1 retrovirus) and comprising an immunodominant epitope of gp41.

These two peptides have the following sequence:

VAU 22 AA

Leu Leu Asn Leu Trp Gly Cys Lys Asn Arg Ala Ile Cys Tyr Thr Ser Val Lys Trp Asn
1 5 10 15 20
Lys Thr
22

VAU 35 AA

Arg Leu Leu Ala Leu Glu Thr Phe Ile Glu Glu Asn Glu Leu Leu Asn Leu Trp Gly Cys
1 5 10 15 20
Lys Asn Arg Ala Ile Cys Tyr Thr Ser Val Lys Trp Asn Lys Thr
25 30 35

For the study, these peptides were used in cyclized form. The results of this study are indicated in Table IV.

Table IV

SERUM	ABSORBANCE				
	PEPTIDE No. 3 (4B)	PEPTIDE No. 2 (3B)	PEPTIDE No. 1 (2B)	VAU 22 AA	VAU 35 AA
ESS*	>**	>	2.494	>	>
DUR*	>	>	>	0.118	0.872
HAD	>	0.518	0.041	0.789	0.871
VAU*	1.342	>	>	>	>
3935	>	0.893	0.307	0.138	0.227
6891	>	0.614	0.062	0.359	0.496
6512*	0.746	0.785	>	0.120	0.174
1105*	1.421	1.031	>	0.099	0.129
4021*	0.430	0.119	>	0.050	1.957
5969*	>	0.282	>	2.491	>
2700	>	0.274	>	>	>
5453	0.555	0.081	>	1.267	1.482
5931	>	>	>	0.202	2.225
3136	>	0.992	0.302	>	>
3653	1.352	>	0.044	1.441	1.322
2352	>	>	0.205	>	>
3016	>	>	0.243	>	>
3302	>	>	0.386	>	>
2294	>	>	0.447	>	>
3771	>	>	0.544	>	>
1581	>	>	>	1.112	0.894
5373	>	>	>	1.359	0.856
7443	>	>	>	0.920	0.574
3637	>	>	>	0.779	1.647
6295*	1.718	1.063	>	0.972	>
6689*	0.710	>	>	>	>
1754	>	>	>	1.263	1.948
4489*	>	>	>	1.318	1.718
4364	>	>	1.382	>	>
3884*	>	>	1.839	>	>
3529	>	>	1.803	>	>
3482	2.402	>	1.473	>	>
1702	>	>	1.162	>	>
6487	>	1.017	2.687	2.889	2.891
5164	>	>	>	>	>
5766*	>	>	>	>	>
3945	>	>	>	>	>

* serotypes / genotypes

** > = signal greater than the reading capacity of the spectrophotometer.

Table IV (continuation)

SERUM	ABSORBANCE				
	PEPTIDE No. 3 (4B)	PEPTIDE No. 2 (3B)	PEPTIDE No. 1 (2B)	VAU-22 AA	VAU 35 AA
4434	>	>	>	2.273	>
4288*	>	>	2.802	2.337	N.T.***
6782	>	2.091	2.462	2.190	2.214
2313	>	>	>	>	>
2312	>	>	>	>	>
1062	>	>	>	>	>
402	>	>	>	>	>
134	>	>	>	>	>
7120	>	>	>	>	>
7212	>	>	>	>	>
6976*	>	>	>	>	>
3600*	>	>	2.743	>	>
3236	>	>	>	>	>
3235	>	>	>	>	>
2551	>	>	>	>	>
5270*	>	>	>	>	>
5210	>	>	>	>	>
5149*	>	>	>	>	>
4477	>	>	>	2.511	>
3891	>	>	2.780	>	>
3627*	>	>	2.910	>	>
7258*	>	>	2.477	>	>
7007	2.136	2.334	>	>	2.151
6697	>	>	>	>	>
6998	>	>	>	>	>
6627	>	>	>	>	>
6198*	>	>	>	>	>
6165	>	>	2.714	>	>
7439	>	>	>	>	>
7297*	>	>	>	>	>
6111	>	>	>	>	>
625	>	>	>	>	2.885

* serotypes / genotypes

** > = signal greater than the reading capacity of the spectro-photometer.

*** Not tested

The results of Table IV demonstrate that peptide No. 3 (4B) exhibits the best performance with regard to that noted for the other peptides. This peptide allows the best discrimination between the sera of patients infected with group O HIV-1 retroviruses compared with the two peptides having a portion of the sequence of the VAU isolate corresponding to the immunodominant epitope of gp41. Moreover, peptide No. 2 (3B) and No. 1 (2B) of the invention are more immunoreactive than the VAU 22 AA peptide which comprises the same number of amino acids.

EXAMPLE 3 :

Evaluation, by an immunoenzymatic test, of the immunoreactivity of the peptides according to the invention: Test No. 2

The serum samples from patients infected with group O HIV-1 retroviruses were obtained by the Yaoundé Pasteur Centre in Cameroon and were serotyped group O according to the serological algorithm described in *AIDS (1977), 11, pp. 445-453*. A genotyped sample (Maryland) is obtained from the United States. These samples were previously diluted in negative human serum at the dilutions given in Table V, in order to have a sufficient volume for the different immunoreactivity tests.

The synthetic peptides used were dissolved in water at a concentration of 1 mg/ml (stock solution). For the solid phase sensitization step ("coating"), the procedure was carried out as described for Example 2.

The serum samples were diluted 1/5 with a skimmed milk solution (citrate buffer supplemented with 0.01% of phenol red, 0.25% of chloroform and 0.25% of Kathon®), deposited in the wells of plates and incubated for 30 min at 40°C.

After washing with a Tris-NaCl buffer solution pH 7.4 containing 0.1% of Tween® 20 and 0.001% of sodium merthiolate, 100 µl of a solution of conjugate consisting of horseradish peroxidase-labelled anti-human IgG and IgM goat antibodies, containing as preservative 0.01% of sodium merthiolate, in solution in a citrate buffer solution supplemented with 30% glycerol and 25% normal foetal calf serum, were added to each well of the plates and then they were incubated for 30 min at 40°C.

After washing with a Tris-NaCl buffer solution pH 7.4 containing 0.1% of Tween® 20 and 0.001% of sodium merthiolate, the colour was developed as described in Example 2.

The relative absorbance (OD) (A490-A620) read in each well is proportional to the immunoreactivity of each peptide. It indicates the ability of each peptide to react with the biological sample with which the test is carried out.

The reactivity of the peptides of the invention, peptides No. 10 (14B), No. 11 (18B), No. 12 (19B), No. 14 (21B), No. 15 (22B), No. 16 (23B) all in cyclized form, was compared with that of three homologous synthetic peptides having, as sequence, a portion of the natural sequence of the envelope (env) of a group O HIV-1 retrovirus. These peptides are two peptides derived from the VAU isolate - the peptide VAU 22 AA and the peptide VAU 35 AA - and the peptide MVP 5180 (designated "MVP 5180" in Table V). The peptides VAU 22 AA and VAU 35 AA (whose structure is indicated in Example 2) and the peptide MVP 5180 comprise an immunodominant epitope of gp41.

All these peptides were used in cyclized form. The sequence of the MVP 5180 peptide is the following:

MVP 5180

Arg Leu Gln Ala Leu Glu Thr Leu Ile Gln Asn Gln Gln Arg Leu Asn Leu Trp Gly Cys
1 5 10 15 20

Lys Gly Lys Leu Ile Cys Tyr Thr Ser Val Lys Trp Asn Thr Ser
25 30 35

The results of this study are indicated in Table V.

Table V

SERUM	PEPTIDES *								
	No. 10	No. 11	No. 12	No. 14	No. 15	No. 16	MVP 5180	VAU 35 AA	VAU 22 AA
	ABSORBANCE (OD)								
4280 at 1/50	0.022	0.686	0.201	0.286	0.689	0.033	0.382	0.013	0.021
NGO at 1/50	0.067	0.335	0.193	0.157	0.315	0.110	0.184	0.055	0.040
NJEM at 1/100	0.032	0.811	0.391	0.277	0.939	0.025	0.146	0.159	0.024
MBASSI at 1/100	1.217	1.150	0.747	2.134	2.010	2.683	0.248	0.120	0.257
WANG at 1/50	0.698	0.234	0.124	2.397	2.680	1.290	0.075	0.025	0.041
258 OUDI at 1/100	0.587	0.373	0.226	0.764	1.184	1.692	0.116	0.058	0.100
DO15 at 1/100	1.613	0.859	1.286	3.357	3.693	3.038	0.673	0.036	0.075
DJOU at 1/100	1.268	0.482	0.419	1.998	2.088	2.166	0.203	0.022	0.042
3600 at 1/100	0.482	0.360	0.249	0.716	0.801	0.933	0.206	0.025	0.058
3613 at ¼00	1.108	0.837	0.773	1.508	1.627	1.679	0.478	0.250	0.396
6111 at 1/100	0.596	0.348	0.202	0.850	1.207	1.009	0.226	0.087	0.180
625 at 1/50	0.838	0.338	0.264	2.045	2.122	1.791	0.202	0.069	0.165
Maryland at ¼00	0.524	0.370	0.285	0.734	0.844	1.229	0.241	0.054	0.168
3653 at 1/10	0.347	0.337	0.247	0.072	0.380	0.406	0.401	0.021	0.310

SOLID PHASE* : PEPTIDE 2 µg/ml

For each peptide tested, the samples were arranged into four classes (a, b, c and d) corresponding to various levels of relative absorbance read at the wavelengths A492-A620 :

- - for a : OD < 0.100,
- - for b : 0.100 < OD < 0.500,
- - for c : 0.500 < OD < 1.000,
- - for d : OD > 1.000,

thus making it possible to evaluate the degree of immunoreactivity of the peptides. The most immunoreactive peptides are those for which the highest number of samples is found in the classes corresponding to the highest absorbance values.

The results are indicated in Table VI.

Table VI

CLASS	PEPTIDES *								
	No. 10	No. 11	No. 12	No. 14	No. 15	No. 16	MVP 5180	VAU 35 AA	VAU 22 AA
	Number of samples								
A	3	0	0	1	0	2	1	11	7
B	2	9	11	3	2	2	12	3	7
C	5	4	2	4	4	1	1	0	0
D	4	1	1	6	8	9	0	0	0

SOLID PHASE* : PEPTIDE 2 µg/ml

The results show that all the peptides of the invention tested achieve a better performance in immunoreactivity than the reference peptides of the prior art which are derived from natural isolates (MVP 5180, VAU). The peptides of the invention No. 15 (22B), No. 14 (21B), and No. 16 (23B) are found to be the most immunoreactive.

EXAMPLE 4 :

Evaluation of the immunoreactivity of the compositions containing peptides according to the invention by an immunoenzymatic test.

For this test, the procedure was carried out according to the protocol described in Example 2 and the same sera were used. The microplates used were sensitized either with peptide No. 1 (2B) cyclized, or with peptide No. 3 (4B) cyclized, or with a composition containing these two peptides (1:1 w/w). Into each well, there were deposited either 100 µl of a solution containing 2 µg/ml of peptide No. 1 (2B), or 100 µl of a solution containing 2 µg/ml of peptide No. 3 (4B), or 100 µl of a solution containing 1 µg/ml of peptide No. 1 (2B) and 1 µg/ml of peptide No. 3 (4B).

The results of this test are given in Table VII.

Table VII

SERUM	ABSORBANCE		
	PEPTIDE No. 1 (2B) (2 µg/ml)	PEPTIDE No. 3 (4B) (2 µg/ml)	PEPTIDE No. 1 (2B) (1µg/ml) + PEPTIDE No. 3 (4B) (1 µg /ml)
3529	1.803	>*	>
1105	>	1.421	>
3891	2.780	>	>
3235	>	>	>
2700	>	>	>
5931	>	>	>
3935	0.307	>	>
7443	>	>	>
1062	>	>	>
1754	>	>	>
3136	0.302	>	>
6891	0.062	>	>
5149	>	>	>
5270	>	>	>
2551	>	>	>
3600	2.743	>	>
6976	>	>	>
4489	>	>	>
6165	2.714	>	>
6198	>	>	>
6627	>	>	>
6998	>	>	>
6697	>	>	>
7258	2.477	>	>
3627	2.910	>	>
4477	>	>	>
3771	0.544	>	>
1702	1.016	>	>
2294	0.447	>	>
2352	0.205	>	>
3016	0.243	>	>
3302	0.386	>	>
3482	1.473	>	>
3653	0.044	1.322	1.105
4364	1.382	>	>
3637	>	>	>
4288	2.802	>	>
5969	>	>	>
258	>	>	>

* > = signal greater than the reading capacity of the spectrophotometer.

Table VII (continued)

SERUM	Absorbance		
	PEPTIDE No. 1 (2B) (2 µg/ml)	PEPTIDE No. 3 (4B) (2 µg/ml)	PEPTIDE No. 1 (2B) (1 µg/ml) + PEPTIDE No.° 3 (4B) (1 µg /ml)
6111	>	>	>
625	>	>	>
6853	>	2.769	>
3136	0.302	>	>
6689	>	0.710	>
6295	>	1.718	>
4021	>	0.430	2.381
3884	1.839	>	>
6512	>	0.746	>
6487	2.687	>	>
ESS	2.494	>	>
HAD	0.041	>	>
DUR	>	>	>

* > = signal greater than the reading capacity of the spectrophotometer.

The results of Table VII demonstrate that the compositions of the peptides of the invention, when used in diagnosis, allow the detection of all the sera from patients infected with group O HIV-1 retroviruses.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:
(A) NAME: Pasteur Sanofi Diagnostics
(B) STREET: 3 boulevard Raymond Poincaré
(C) CITY: Marnes la Coquette
(E) COUNTRY: France
(F) POSTAL CODE (ZIP): 92430
(G) TELEPHONE: 0153774000
(H) TELEFAX: 0153774133

(ii) TITLE OF INVENTION : Synthetic peptides which can be used in biological tests for the detection of infections due to the group O HIV-1 virus

(iii) NUMBER OF SEQUENCES: 16

(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Ser Thr
20

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Ser Thr
20

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

Val Gln Trp Asn Glu Thr
20

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser
1 5 10 15

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly
1 5 10 15

Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly
1 5 10 15

Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly
1 5 10 15

Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:
(A) ORGANISM: syn

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

```
Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu
1               5                  10                  15

Val Cys Tyr Thr Ser Val
            20
```

CLAIMS

1. Synthetic peptides of the monomer type with 13 to 33 amino acids or of the dimer type with 26 to 66 amino acids, in linear form or in a form cyclized by means of inter-cysteine disulphide bridges, corresponding to the general formula (I):

$$\Delta\text{-Z-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega \qquad (I)$$

in which :

-Δ represents a biotinyl radical, a biocytinyl radical, a hydrogen atom, an acetyl (CH_3CO-) radical, an aliphatic chain which may contain one or two thiol, aldehyde or amine functional groups, the aliphatic chain preferably being an alkyl chain of 1 to 6 carbon atoms or an alkenyl chain of 2 to 6 carbon atoms, or an aminoalkylcarbonyl chain of 2 to 6 carbon atoms,

-Z represents a peptide sequence of one of the formulae (II) to (X) :

$-\Xi_1$-Ser-Ξ_2-	(II)
-Ser-Ξ_2-	(III)
$-\Xi_1$-Ser-	(IV)
$-\Xi_1$-Gln-Ξ_2-	(V)
-Gln-Ξ_2-	(VI)
$-\Xi_1$-Gln-	(VII)
$-\Xi_1$-Asn-Ξ_2-	(VIII)
-Asn-Ξ_2-	(IX)
Ξ_1-Asn-	(X)

in which :

-Ξ_1 represents a peptide sequence of 0 to 9 amino acids and

-Ξ_2 represents a peptide sequence of 0 to 5 amino acids,

-Θ represents a peptide sequence of formula (XI):

$-(AA_1)-(AA_2)-(AA_3)-(AA_4)-(AA_5)-$ (XI)

in which :

- (AA_1) represents either a lysine residue, or an arginine residue, or an ornithine residue,
- (AA_2) represents either a glycine residue, or an asparagine residue,
- (AA_3) represents either a lysine residue, or an arginine residue, or an ornithine residue,
- (AA_4) represents either a leucine residue, or an alanine residue, or an isoleucine residue, or a glutamine residue,
- (AA_5) represents either an isoleucine residue, or a valine residue, or a leucine residue, or a threonine residue, or a norleucine residue, or a norvaline residue,

provided, however, that (AA_1), (AA_2), (AA_3), (AA_4) and (AA_5) never form together the peptide sequences -Lys Gly Lys Leu Ile- and -Lys Gly Lys Leu Val-,

-Ω, attached to the -CO- group of serine, represents:

- a hydroxyl (-OH) radical or an amino ($-NH_2$) radical,
- an alkoxy radical comprising from 1 to 6 carbon atoms,
- a peptide sequence of formula (XII) :

$-Val-\Sigma-\Psi$ (XII)

in which Σ represents a sequence of formula (XIII) or of formula (XIV) :

$-(AA_6)-Trp\ Asn-(AA_7)-(AA_8)$ (XIII)

$-(AA_6)-Trp\ His-(AA_7)-(AA_8)$ (XIV)

in which :

- (AA_6) represents an amino acid different from lysine,
- (AA_7) represents an amino acid,
- (AA_8) represents a serine or threonine residue,

and Ψ, attached to the -CO- residue of the free AA_8 amino acid, represents an OH or NH_2 group or an alkoxy radical comprising from 1 to 6 carbon atoms,

- a peptide sequence of formula (XV) :

-Val-Ψ (XV)

in which Ψ, attached to the -CO- residue of valine, has the same meaning as for the formula (XII),

- or a peptide sequence of formula (XVI) to (XVIII) :

-Z-TrpGlyCys-Θ-CysTyrThrSer-Ψ (XVI)

Val-Σ-Z-TrpGlyCys-Θ-CysTyrThrSerVal-Σ-Ψ (XVII)

Val-Z-TrpGlyCys-Θ-CysTyrThrSerVal-Ψ (XVIII)

in which Z and Θ have the definition given for the formula (I) and Σ has the definition given for the formula (XII) and Ψ, attached to the -CO- residue of serine, on the -CO- residue of the AA_8 amino acid or on the -CO- residue of valine, has the same meaning as for the formula (XII).

2. Synthetic peptides of formula (I) according to Claim 1, in which (AA_5) represents either a valine residue, or a leucine residue, or a threonine residue and when Ω corresponds to a peptide sequence of formula (XII) or (XIV), (AA_6) represents either a glutamine residue or an arginine residue.

3. Synthetic peptides of formula (I), according to Claim 1, in which:

-Δ represents a biotinyl radical, a hydrogen atom or an aliphatic chain which may contain one or two thiol, aldehyde or amine functional groups, the aliphatic chain preferably being an alkyl chain of 1 to 6 carbon atoms, or an aminoalkylcarbonyl chain of 2 to 6 carbon atoms,

-Z represents a peptide sequence of formula (II) or (V), in which Ξ_1 represents a peptide sequence of two amino acids and Ξ_2 represents an amino acid, or a sequence of formula (IV), in which Ξ_1 represents three amino acids, or a peptide sequence of formula (VIII), in which Ξ_1 represents a peptide sequence of nine, eight or three amino acids and Ξ_2 a

peptide sequence of five amino acids,

-Θ represents a peptide sequence of formula:

-Lys Gly Arg Leu Val-,

-Arg Gly Lys Ala Val-,

- Arg Gly Arg Leu Val-,

or

-Arg Gly Arg Ala Val-,

and

-Ω represents a hydroxyl group, the peptide sequence (XV) or one of the following sequences which correspond to the peptide sequence of formula (XII) :

- Val Arg Trp Asn Glu Thr-Ψ,

- Val Gln Trp Asn Glu Thr-Ψ

or

- Val Gln Trp Asn Ser Thr-Ψ.

4. Synthetic peptides of formula (I), according to one of Claims 1 to 3, in which Z represents a peptide sequence of formula:

- -Leu Leu Ser Ser-
- -Leu Leu Asn Ser-
- -Arg Leu Asn Ser-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu-
- -Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile-
- -Leu Asn Gln Gln Arg Leu Leu Asn Ser-

or

- -Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser-

5. Synthetic peptides of 20 to 50 amino acids according to Claim 1, of formula (Ia):

$$\Delta\text{-}Z_a\text{-TrpGlyCys-}\Theta\text{-CysTyrThrSer-}\Omega_a \qquad \text{(Ia)}$$

in which Z_a represents a radical of formulae IIa to Xa :

Ξ_{1a}-Ser-Ξ_{2a}	(IIa)
-Ser-Ξ_{2a}	(IIIa)
-Ξ_{1a}-Ser	(IVa)
Ξ_{1a}-Gln-Ξ_{2a}	(Va)
-Gln-Ξ_{2a}	(VIa)
Ξ_{1a}-Gln-	(VIIa)
Ξ_{1a}-Asn-Ξ_{2a}	(VIIIa)
-Asn-Ξ_{2a}	(IXa)
-Ξ_{1a}-Asn	(Xa)

in which :

-Ξ_{1a} represents a peptide sequence of 1 to 5 amino acids and

-Ξ_{2a} an amino acid,

-Ω_a represents a peptide sequence of formula (XII), as defined for the formula (I), or a peptide sequence of formula (XVIIa) :

Val-Σ-Z_a-TrpGlyCys-Θ-CysTyrThrSerVal-Σ-Ψ (XVIIa)

and

Δ, Θ, Σ and Ψ have the same meaning as for the formula (I).

6. Synthetic peptides of formula (I) according to one of Claims 1 to 5 including one of the following sequences:

Sequence No. 1

-LLSLWGCRGKAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 2

-LLSLWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 3

-LLSSWGCKGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 4

-LLSSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr-
22

Sequence No. 5

-LLQSWGCKGRLVCYTSVQWNST-

or

-Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu alV Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr-
22

Sequence No. 6

-LLNSWGCRGKAVCYTSVQWNET-

or

-Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 7

-LLSLWGCRGRAVCYTSVQWNET-

or

-Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 8

-LLSSWGCRGRLVCYTSVQWNET-

or

-Leu Leu Ser Ser Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr-
22

Sequence No. 9 :

-LLSSWGCKGRLVCYTS-

or

-Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-
1 5 10 15

Sequence No. 10 :

-LLNSWGCKGRLVCYTS-

or

-Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser-
1 5 10 15

Sequence No. 11 :

-ALETLLQNQQLLNSWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ser Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-
20 25 30

Sequence No. 12 :

-ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-
20 25 30

Sequence No. 13 :

-ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET-

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr-
20 25 30

Sequence No. 14 :

-LNQQRLLNSWGCKGRLVCYTSV-

or

-Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr
1 5 10 15
Thr Ser Val-
20

Sequence No. 15 :

-RALETLLNQQRLLNSWGCKGRLVCYTSV-

or

- Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys
1 5 10 15
Gly Arg Leu Val Cys Tyr Thr Ser Val-
20 25

Sequence No. 16 :

-RLNSWGCKGRLVCYTSV-

or

- Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val-
1 5 10 15

7. Synthetic peptides, according to one of Claims 1 to 6, of sequence:

PEPTIDE No. 1 (2B)

LLSLWGCRGKAVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 2 (3B)

LLSLWGCRGRLVCYTSVQWNET

or

Leu Leu Ser Leu Trp Gly Cys Arg Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 3 (4B)

LLSSWGCKGRLVCYTSVQWNET

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE No. 4 (5B)

LLSSWGCKGRLVCYTSVQWNST

or

Leu Leu Ser Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr
22

PEPTIDE No. 5 (6B)

LLQSWGCKGRLVCYTSVQWNST

or

Leu Leu Gln Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Ser Thr
22

PEPTIDE No. 6

LLNSWGCRGKAVCYTSVQWNET

or

Leu Leu Asn Ser Trp Gly Cys Arg Gly Lys Ala Val Cys Tyr Thr Ser Val Gln Trp Asn
1 5 10 15 20
Glu Thr
22

PEPTIDE NO. 12 (19B)

ALETLLQNQQLLNIWGCRGRLVCYTSVRWNET

or

Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asn Ile Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE No. 13 (20B)

ALETLLQNQQLLDLWGCRGRLVCYTSVRWNET

or

-Ala Leu Glu Thr Leu Leu Gln Asn Gln Gln Leu Leu Asp Leu Trp Gly Cys Arg Gly
1 5 10 15
Arg Leu Val Cys Tyr Thr Ser Val Arg Trp Asn Glu Thr
20 25 30

PEPTIDE No. 14 (21B)

LNQQRLLNSWGCKGRLVCYTSV

or

Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr
1 5 10 15
Thr Ser Val
20

PEPTIDE No. 15 (22B)

RALETLLNQQRLLNSWGCKGRLVCYTSV

or

Arg Ala Leu Glu Thr Leu Leu Asn Gln Gln Arg Leu Leu Asn Ser Trp Gly Cys Lys
1 5 10 15
Gly Arg Leu Val Cys Tyr Thr Ser Val
20 25

PEPTIDE No. 16 (23B)

RLNSWGCKGRLVCYTSV

or

Arg Leu Asn Ser Trp Gly Cys Lys Gly Arg Leu Val Cys Tyr Thr Ser Val

8. Composition containing one or more synthetic peptides of formula (I) according to any one of Claims 1 to 7.

9. Composition according to Claim 8, containing peptide No. 3 (4B) and peptide No. 1 (2B).

10. Composition containing one or more synthetic peptides of formula (I) according to Claim 1 and one or more group O HIV-1 recombinant peptides.

11. Composition containing one or more synthetic peptides of formula (I), according to Claim 1, and one or more HIV-1 and/or HIV-2 recombinant or synthetic peptides.

12. Immunoassay method using one or more synthetic peptides of formula (I), according to any one of Claims 1 to 7.

13. Immunoassay method using a composition according to any one of Claims 8 to 11.

14. Diagnostic kit including at least one synthetic peptide of formula (I), according to any one of Claims 1 to 7, or a composition according to any one of Claims 8 to 11.

ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION,
NON PRIORITY; OR PROVISIONAL APPLICATIONS

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DECLARATION AND POWER OF ATTORNEY U.S.A.

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ATTORNEY'S DOCKET NO

P63163US0

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or a first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

101 **SYNTHETIC PEPTIDES USEFUL IN BIOLOGICAL ASSAYS FOR DETECTING INFECTIONS CAUSED BY GROUP O HIV-VIRUSES**

102 which is described and claimed in.
- ☐ the attached specification
- ☒ the specification in application (if applicable) and

☒ PCT International Application No. **PCT/FR98/00691** filed **6 April 1998**

filed **8 December 1998**

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1 56
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

103 Prior Foreign Application(s)

(Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed Yes	No
97 04 356	France	9 April 1997	☒	☐
98 02 212	France	24 February 1998	☒	☐
			☐	☐

104 I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105 I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status patented, pending, abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith. HARVEY B. JACOBSON JR. (20,851); D. DOUGLAS PRICE (24,514); JOHN CLARKE HOLMAN (22,769); MARVIN R. STERN (20,640); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007); WILLIAM E. PLAYER (31,409)

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*Inventor(s) name must include at least one unabbreviated first or middle name.

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further declare that all statements made herein of my own knowledge are true and that all statement made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201 *	SIGNATURE OF INVENTOR 202 *	SIGNATURE OF INVENTOR 203 *
DATE February 10, 1999	DELAGNEAU Jean-François Hubert DATE February 10, 1999	GADELLE Stéphane Jean Xavier DATE February 10, 1999
CHENEBAUX Denis Marie Bernard		

Additional inventors are named on separately numbered sheets attached hereto.

JACOBSON, PRICE, HOLMAN & STERN, PLLC
ADDITIONAL INVENTORS

* Inventor(s) name must include at least one unabbreviated first or middle name.

204	FULL NAME * OF INVENTOR	FAMILY NAME 4-00 RIEUNIER	GIVEN NAME ~~Francois Yves~~	MIDDLE NAME	
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	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
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	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
210	FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
211	FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 204 * RIEUNIER ~~Francois~~ Yves	SIGNATURE OF INVENTOR 205 *	SIGNATURE OF INVENTOR 206 *
DATE February 10, 1999	DATE	DATE
SIGNATURE OF INVENTOR 207 *	SIGNATURE OF INVENTOR 208 *	SIGNATURE OF INVENTOR 209 *
DATE	DATE	DATE
SIGNATURE OF INVENTOR 210 *	SIGNATURE OF INVENTOR 211 *	
DATE	DATE	

□ Additional inventors are named on separately numbered sheets attached hereto.